

CLAIMS

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We claim:

1. A method of diagnosing decreased vascular function in a subject,
comprising
assaying the number of endothelial progenitor cells in a blood sample from
10 the subject, wherein a decrease in the number of endothelial progenitor cells in the
sample as compared to a control indicates decreased vascular function.
2. The method of claim 1, wherein assaying the number of endothelial
progenitor cells comprises
15 isolating the buffy coat from a blood sample of the subject;
culturing the buffy coat on a solid support coated with a first substrate;
isolating the non-adherent cells;
culturing the non-adherent cells on a solid support coated with a second
substrate;
20 counting the number of colonies on the solid support.
3. The method of claim 2, wherein a lower number of colonies on the solid
support as compared to a control indicates decreased vascular function.
- 25 4. The method of claim 1, wherein assaying the number of endothelial
progenitor cells comprises
determining the number of VEGFR²⁺CD31^{hi} cells in the sample.
5. The method of claim 1, wherein the control is a blood sample from a
30 subject that does not have atherosclerosis.
6. The method of claim 1, wherein the control is a standard value.
7. The method of claim 2, wherein the first substrate comprises fibronectin.

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8. The method of claim 2, wherein the first and the second substrate comprise fibronectin.

5 9. A method of diagnosing increased vascular function in a subject, comprising

 assaying the number of endothelial progenitor cells in a blood sample from the subject, wherein an increase in the number of endothelial progenitor cells in the sample as compared to a control indicates decreased vascular function.

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 10. The method of claim 9, wherein the subject has been treated with a cholesterol-lowering agent.

 11. The method of claim 10, wherein the control is a blood sample from the
15 subject prior to treatment with the cholesterol-lowering agent.

 12. The method of claim 9, wherein assaying the number of endothelial progenitor cells comprises

 isolating the buffy coat from a blood sample of the subject;
20 culturing the buffy coat on a solid support coated with a first substrate;
 isolating the non-adherent cells;
 culturing the non-adherent cells on a solid support coated with a second substrate;
 counting the number of colonies on the solid support.

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 13. The method of claim 12, wherein a higher number of colonies on the solid support as compared to a control indicates increased vascular function.

 14. The method of claim 12, wherein the first substrate comprises
30 fibronectin.

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15. The method of claim 12, wherein the first substrate and the second substrate comprises fibronectin.

16. The method of claim 9, wherein assaying the number of endothelial progenitor cells comprises
5 determining the number of VEGFR²⁺CD31^{hi} cells in the sample.

17. A method of treating a subject with decreased vascular function, comprising,
10 administering to the subject a therapeutically effective amount of endothelial progenitor cells, thereby increasing vascular function in the subject.

18. The method of claim 17, wherein the subject has atherosclerosis.

19. The method of claim 17, wherein the endothelial progenitor cells are VEGFR²⁺CD31^{hi} cells.

20. A method for screening for an agent that affects vascular function, comprising
20 administering a therapeutically effective amount of the agent to a subject, and
assessing the number of endothelial progenitor cells in a sample from the subject;
wherein an increased number of endothelial progenitor cells in the sample as
25 compared to a control indicates that the agent affects vascular function.

21. The method of claim 20, wherein the subject is a non-human animal.

22. The method of claim 22, wherein the subject is a human.

30 23. The method of claim 20, wherein the agent is a cholesterol lowering agent.

24. The method of claim 20, wherein the control is the number of circulating endothelial cell in sample from a subject not administered the agent.

5 25. The method of claim 20, wherein the sample is a blood sample.

26. The method of claim 20, wherein the sample is a buffy coat sample.

27. The method of claim 20, wherein the endothelial progenitor cells are
10 circulating endothelial progenitor cells.

28. The method of claim 20, wherein assaying the number of endothelial progenitor cells comprises

isolating the buffy coat from a blood sample of the subject;
15 culturing the buffy coat on a solid support coated with a first substrate;
isolating the non-adherent cells;
culturing the non-adherent cells on a solid support coated with a second
substrate;
enumerating the number of colonies on the solid support.

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29. The method of claim 20, wherein assaying the number of endothelial progenitor cells comprises

determining the number of VEGFR²⁺CD31^{hi} cells in the sample.

25 30. A method for screening for an agent of use in treating a cardiovascular disease, comprising

administering a therapeutically effective amount of the agent to a subject,
and

assessing the number of endothelial progenitor cells in a sample from the
30 subject;

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wherein an increased number of endothelial progenitor cells in the sample as compared to a control indicates that the agent is of use in treating the cardiovascular disease.

5 31. The method of claim 30, wherein the subject is a non-human animal.

32. The method of claim 30, wherein the subject is a human.

33. The method of claim 30, wherein the agent is a cholesterol lowering
10 agent.

34. The method of claim 30, wherein the control is the number of circulating endothelial cell in sample from an animal not administered the agent.

15 35. The method of claim 30, wherein the sample is a blood sample.

36. The method of claim 30, wherein the sample is a buffy coat sample.

37. The method of claim 30, wherein the endothelial progenitor cells are
20 circulating endothelial progenitor cells.

38. The method of claim 20, wherein assaying the number of endothelial progenitor cells comprises

isolating the buffy coat from a blood sample of the subject;
25 culturing the buffy coat on a solid support coated with a first substrate;
isolating the non-adherent cells;
culturing the non-adherent cells on a solid support coated with a second
substrate;
enumerating the number of colonies on the solid support.

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39. The method of claim 20, wherein assaying the number of endothelial progenitor cells comprises

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determining the number of VEGFR²⁺CD31^{hi} cells in the sample.

40. A method of diagnosing increased cardiovascular risk in a subject, comprising

5 assaying the number of endothelial progenitor cells in a blood sample from the subject,

 wherein a decrease in the number of endothelial progenitor cells in the sample as compared to a control indicates increased cardiovascular risk.

10 41. The method of claim 40, wherein assaying the number of endothelial progenitor cells comprises

 isolating the buffy coat from a blood sample of the subject;

 culturing the buffy coat on a solid support coated with a first substrate;

 isolating the non-adherent cells;

15 culturing the non-adherent cells on a solid support coated with a second substrate;

 enumerating the number of colonies on the solid support.

20 42. The method of claim 41, wherein a lower number of colonies on the solid support as compared to a control indicates decreased vascular function.

 43. The method of claim 41, wherein assaying the number of endothelial progenitor cells comprises

25 determining the number of VEGFR²⁺CD31^{hi} cells in the sample.

 44. The method of claim 41, wherein the control is a blood sample from a subject that does not have atherosclerosis.

30 45. The method of claim 41, wherein the control is a standard value.

 46. The method of claim 42, wherein the first substrate comprises fibronectin.

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47. The method of claim 42, wherein the first and the second substrate comprise fibronectin

5 48. A method of diagnosing increased cardiovascular risk or decreased vascular function in a subject, comprising

 assaying a number of senescent endothelial progenitor cells in a blood sample from the subject,

 wherein an increase in the number of senescent endothelial progenitor cells
10 in the sample as compared to a control indicates increased cardiovascular risk or decreased vascular function.

 49. The method of claim 48, wherein the control is a standard value.

15 50. The method of claim 48, wherein the control is a number of senescent endothelial progenitor cells in a blood sample from a subject known not to be affected by a disease or disorder.

 51. A method for screening for an agent of use in treating a cardiovascular
20 disease, comprising

 administering a therapeutically effective amount of the agent to a subject,
 and

 assessing the number of senescent endothelial progenitor cells in a sample from the subject;

25 wherein a decreased number of senescent endothelial progenitor cells in the sample as compared to a control indicates that the agent is of use in treating the cardiovascular disease.

 52. The method of claim 51, wherein the control is a standard value.

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53. The method of claim 51, wherein the control is a number of senescent endothelial progenitor cells in a blood sample from a subject known to be affected by a disease or disorder.